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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/770,291	02/02/2004	Yihong Qiu	6437.US.C5	2213
23492	7590	09/18/2007	EXAMINER	
ROBERT DEBERARDINE			GHALI, ISIS A D	
ABBOTT LABORATORIES				
100 ABBOTT PARK ROAD			ART UNIT	
DEPT. 377/AP6A			PAPER NUMBER	
ABBOTT PARK, IL 60064-6008			1615	
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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<b>Office Action Summary</b>	Application No. 10/770,291	Applicant(s) QIU ET AL.	
	Examiner Isis A. Ghali	Art Unit 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_\_.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 16 and 19 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 16 and 19 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
     If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
     a) ☐ All    b) ☐ Some \* c) ☐ None of:  
         1. ☐ Certified copies of the priority documents have been received.  
         2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
         3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
     \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
     a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                       | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                              | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>6/4/04</u> . | 6) <input type="checkbox"/> Other:  |

### **DETAILED ACTION**

The receipt is acknowledged of applicants' preliminary amendment and IDS filed 06/04/2004; and supplemental amendment and IDS filed 07/09/2004.

Claims 1-5, 17 and 18 have been canceled, and claim 19 has been added.

Claims 16 and 19 are pending and included in the prosecution.

### ***Claim Rejections - 35 USC § 112***

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 16 and 19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for very specific oral formulations having specific ingredients to deliver divalproex sodium, does not reasonably provide enablement for any pharmaceutical formulation comprising any valproate compounds as currently recited by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: the nature of the invention; the breadth of the claims; the state of the prior art; the relative skill of those in the art; the amount of direction or guidance presented; the predictability or unpredictability of the art; the presence or absence of working examples; and the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

**The nature of the invention:** The nature of the invention as claimed is a hydrophilic matrix formulation comprising valproate compounds for once a day administration.

**The breadth of the claims:** The claims are broad. The claims encompass myriad of hydrophilic matrix formulations including transdermal and implant formulations comprising valproate compounds.

**The state of the prior art:** The state of the art does not recognize once a day transdermal or implantable formulations comprising valproate compounds. The state of the art recognizes once a day oral administration of divalproex sodium in a pharmaceutical formulation, see US 4,913,906.

**The relative skill of those in the art:** The relative skill of those in the art is high.

**The amount of direction or guidance presented:** The specification provides no guidance, in the way written description, on any formulations other than oral formulation,

and provides no guidance of any valproate compounds other than divalproex sodium. In page 12, under the heading "Dosage Forms", applicants stated that:

"Matrix systems are well known in the art. In a matrix system, the drug is homogenously dispersed in a polymer in association with conventional excipients. This admixture is typically compressed under pressure to produce a tablet. Drug is released from this tablet by diffusion and erosion."

In page 6, applicants disclosed the claimed dissolution profile, and stated that "Upon ingestion, a formulation meeting this profile produced  $C_{max}$ ,  $C_{min}$ , and AUC describe above". This disclosure emphasizes that the claimed dissolution profile is obtained by oral administration of the hydrophilic matrix.

In example 1, pages 20-22, applicants disclosed very specific oral hydrophilic matrix formulations containing divalproex sodium as shown by table 4 at page 27.

It is not obvious from the disclosure of specific oral hydrophilic matrix tablet formulation comprising specific ingredients in specific amounts containing specific amount of divalproex sodium if all other matrix formulations such as transdermal or implant will work to deliver valproate compound to provide the same effect. The claimed dissolution profile is the result of the described specific hydrophilic matrix formulation. *In re Dreshfield*, 110 F.2d 235, 45 USPQ 36 (CCPA 1940), gives this general rule: "It is well settled that in cases involving chemicals and chemical compounds, which differ radically in their properties it must appear in an applicant's specification either by the enumeration of a sufficient number of the members of a group or by other appropriate language, that the chemicals or chemical combinations included in the claims are capable of accomplishing the desired result. A disclosure should contain representative

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examples which provide reasonable assurance to one skilled in the art that the formulations fall within the scope of a claim will possess the alleged activity. See *In re Riat et al.* (CCPA 1964) 327 F2d 685, 140 USPQ 471; *In re Barr et al.* (CCPA 1971) 444 F 2d 349, 151 USPQ 724.

**The predictability or unpredictability of the art:** The lack of guidance from the specification and from the prior art with regard to formulations comprising valproate compounds administered transdermally, as implant, or parentally makes practicing the claimed invention unpredictable in the terms of administering valproate compounds by other formulations by other routes such as transdermally or parentally.

**The presence or absence of working examples:** The specification discloses only very specific oral hydrophilic matrix formulation comprising divalproex sodium, pages 6, 12, and example 1. No working examples to show formulations other than the disclosed oral hydrophilic matrix formulation. Therefore, the specification has enabled only oral hydrophilic matrix formulations having specific ingredients to deliver divalproex sodium.

**The quantity of experimentation necessary:** The art and the specification demonstrate oral hydrophilic matrix formulation of divalproex sodium. Therefore, the practitioner would turn to trial and error experimentation to practice the instant composition for delivering formulation other than oral to deliver valproate compounds without guidance from the specification or the prior art. Therefore, undue experimentation becomes the burden of the practitioner.

### ***Double Patenting***

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 16 and 19 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 6,419,953.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims and the claims of the issued patent are directed to formulation comprising valproate compounds. The issued claims anticipate the present claims since the presently claimed dissolution profile is inherent.

5. Claims 16 and 19 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6,511,678.

Although the conflicting claims are not identical, they are not patentably distinct from

each other because the present claims and the claims of the issued patent are directed to formulation comprising valproate compounds. The issued claims anticipate the present claims since the presently claimed dissolution profile is inherent.

6. Claims 16 and 19 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 6,528,090. Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims and the claims of the issued patent are directed to formulation comprising valproate compounds. The issued claims anticipate the present claims since the presently claimed dissolution profile is inherent.

7. Claims 16 and 19 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2 of U.S. Patent No. 6,528,091. Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims and the claims of the issued patent are directed to formulation comprising valproate compounds. The issued claims anticipate the present claims since the presently claimed dissolution profile is inherent.

8. Claims 16 and 19 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 6,720,004. Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims and the claims of the issued patent are directed



to formulation comprising valproate compounds. The issued claims anticipate the present claims since the presently claimed dissolution profile is inherent.

9. Claims 16 and 19 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-17 of U.S. Patent No. 6,713,086. Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims and the claims of the issued patent are directed to formulation comprising valproate compounds. The issued claims anticipate the present claims since the presently claimed dissolution profile is inherent.

10. Claims 16 and 19 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 46-59 of copending Application No. 10/770,290. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter claimed in the instant application is fully disclosed in the referenced copending applications and would be covered by any patent granted on the copending applications since the referenced copending applications and the instant application are claiming common subject matter as follows: formulation comprising valproate compounds. The present claims and the conflicting claims in the copending application anticipate each other since pharmacokinetics and dissolution profile are inherent.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

***Claim Rejections - 35 USC § 102***

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 16 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by article "EPILIM CHRONO: A MULTIDOSE, CROSSOVER COMPARISON OF TWO FORMULATIONS OF VALPROATE IN HEALTHY VOLUNTEERS", by Roberts et al.

The present claims are directed to hydrophilic matrix formulation comprising valproate compounds administered once a day.

Roberts et al. disclosed once a day controlled release formulation to deliver divalproex sodium: Epilim Chrono. Epilim Chrono comprises valproate compounds and hydrophilic polymer "ethylcellulose as evident by patient information leaflet of the product. Epilim Chrono is also in the form of a matrix formulation because matrix, as defined by applicants in page 12, "the drug is homogeneously dispersed in the polymer". Roberts et al. provided comparison between once a day formulation and twice daily controlled formulation. The comparison showed once a day formulation of 1000 mg is almost identical to the enteric coated twice a day formulation. The dissolution profile is inherent to a specific formulation.

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13. Claims 16 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by US 4,913,906 (906).

US '906 disclosed composition for controlled release of salts of valproic acid comprising 10-80% of the active agent (abstract; col.2, lines 1-10, 63-68). The controlled release formulation results in sustained action of the drug with small fluctuation of the plasma level over prolonged period of time (col.1, lines 59-62). The composition is a once a day oral formulation that delivers the drug for 24 hour and shows about 97% dissolution rate profile after 24 hr. (col. 5 and 6, tables 1-4). Divalproex sodium is disclosed as one of the salts of valproic acid suitable for the formulation of the reference (col.5, lines 15-20). The dissolution profile is inherent for the formulation. In absence of claiming a specific formulation, the prior art anticipated the claims.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis A. Ghali whose telephone number is (571) 272-0595. The examiner can normally be reached on Monday-Thursday, 7:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373.. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

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published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should

you have questions on access to the Private PAIR system, contact the Electronic

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USPTO Customer Service Representative or access to the automated information

system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Isis A Ghali  
Primary Examiner  
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IG

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